REMARKS

Claims 32, 34-37, 40, and 41 will be pending.

There has been no response to applicants paper of December 27, 2004. The Examiner is called upon to address it.

Further, in the course of the telephone interview referred to, i.e., the December 14, 2004 interview, the Examiner was called upon to present evidence to support her position that fragments of 3 amino acids generate B cell responses. During that interview, applicants were told that the Examiner would either present the support or withdraw the rejection. The rejection has not been withdrawn, nor has the Examiner provided the relevant support which was promised. Why not?

Claims 32, 35, 36, and 41 are pending. Claim 32, as amended, combines claim 33 therein. The claims thus require the protein recited therein to be converted to a molecule which, when complexed to an MHC molecule, generates a T cell response.

In view of the amendment of claim 32, any and all of the Examiner's remarks regarding antibodies and B cells are irrelevant. Indeed, applicants stated during the interview that they would, in fact, amend the claims to refer only to T cells.

The Examiner's rejection is based upon the premise that binding to an MHC molecule alone is not sufficient to generate a T cell response. To elaborate, a peptide molecule must both bind to an MHC molecule, and following this, engage a T cell receptor in order to stimulate the proliferation of T cells.

This is absolutely correct; however, what is NOT correct is the reasoning which follows the Examiner's recognition of these facts.

The claims all refer to a molecule that is, in fact 752 amino acids long. This molecule, i.e., "NY-ESO-1," is subject to the same rules of MHC binding as are all peptides. In order for a peptide to bind to an MHC molecule, it must satisfy certain criteria. These criteria are well known. Reference is made, for example, to the references cited at page 25 of the specification. The Examiner is also invited to review a reference work such as Marsh, et al., The HLA Facts Book (Academic Press, 2000). The

point is, if one is looking for, e.g., a peptide which can be found in SEQ ID NO: 1, which will bind to, e.g., an HLA-B8 molecule, and will generate a T cell response, one's choices are limited. The analysis using the referenced motifs identified three. Granted these three peptides were not listed for T cell proliferation, but this is an enablement issue, rather than one of written description. The Examiner appears to accept the contention that, using the incorporated references and the sequence of SEQ ID NO: 1, one can identify the peptides which bind to an HLA molecule. The issue then is: do these identified peptides which bind, provoke a proliferative T cell response; however, there is no such rejection.

The Examiner states that

> "(T)he instant specification may provide an adequate written description of the claimed immunoreactive portion, per Lilly (i.e., University of California v. Eli Lilly & Co., 43 USPQ2d (Fed. Cir. 1997)), by structurally describing a representation number of immunoreactive portions, or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus."

(emphasis added). Applicants do not agree that Lilly is controlling in the present case. In Lilly, no sequences for human insulin were provided. Such is not the case here, where peptides which the Examiner finds allowable are described, where the peptides were identified precisely as described in the specification. Examiner 12 describes how motif analysis was carried out using D'Amaro and Drijfhout. See page 24, lines 7 and 9. Note that "Peptides corresponding to all the amino acids deduced thereby were synthesized." These were then listed. SEQ ID NOS: 4, 5, and 6 were the three best peptides, with respect to binding to HLA-A2, and provoking T cell proliferation.

If the methodology worked for HLA-A2, why would it not work for HLA-A1? Or HLA-A3? Or HLA-B7? Or HLA-B35? Or any MHC molecule? The Examiner has not provided any basis for her position, and has in fact pointed out that there is ample support within applicants specification to support the claims.

In fact, a number of T cell epitopes have been identified for peptides with sequences found in SEQ ID NO: 1. A list of these, with their HLA binder and the reference so describing them, is attached. This certainly contradicts the Examiner's position.

Withdrawal of the rejection, and allowance of claims 32, 34-37, 40, and 41 is proper and is urged.

Respectfully submitted,

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Attachment: T Cell List

T cell epitope peptides derived from NY-ESO-1

HLA	Sequence	Position	Reference
A2	SLLMWITQC	157-165	Jager, 1998 Chen, 2000 Valmori, 2000
A24	LLMWITQCF	158-166	Yamaguchi 2004
A31	ASGPGGGAPR	53-62	Wang, 1998
B35	MPFATPMEA	94-102	Benlalam, 2003
B51	MPFATPMEA	94-102	Jäger, 2002
Cw3	LAMPFATPM	92-100	Gnjatic, 2000
Cw6	ARGPESRLL	80-88	Gnjatic, 2000
DP4	SLLMWITQCFLPVF	157-170	Zeng, 2001
DR4	PGVLLKEFTVSGNILTIRLT	119-138	Jager, 2000 Zarour, 2000
DR4	VLLKEFTVSG	121-130	Zeng, 2000
DR4	AADHRQLQLSISSCLQQL	139-156	Jager, 2000
DR7	PGVLLKEFTVSGNILTIRLTAADHR	119-143	Zarour, 2002

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